

## Solid Tumour Section

### Mini Review

# Soft tissue tumors: Dermatofibrosarcoma protuberans

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## Identity

### Alias

Dermatofibrosarcoma Protuberans  
Darier Ferrand tumor  
Darier-Hoffmann tumor

### Note

t(17;22)(q22;q13) is found in most if not all Dermatofibrosarcoma Protuberans cases.

## Clinics and pathology

### Disease

Neoplasm of the deep dermis with extension to the subcutis, characterized by locally aggressive

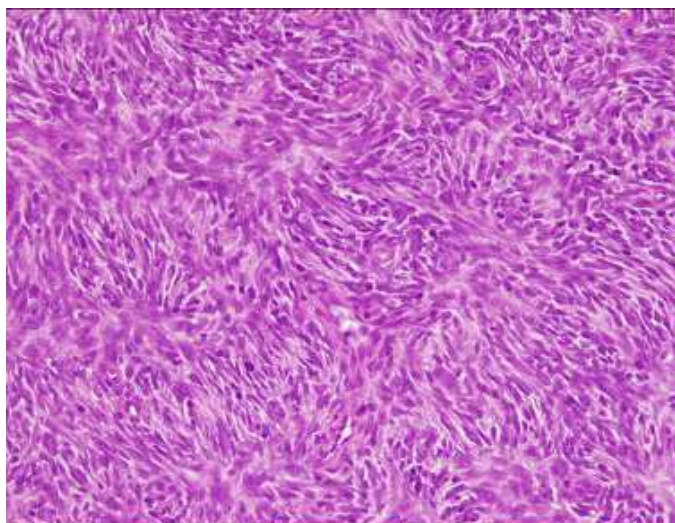
growth. Dermatofibrosarcoma Protuberans (DFSP) is primarily associated with the trunk, limbs, head, neck and vulva.

### Epidemiology

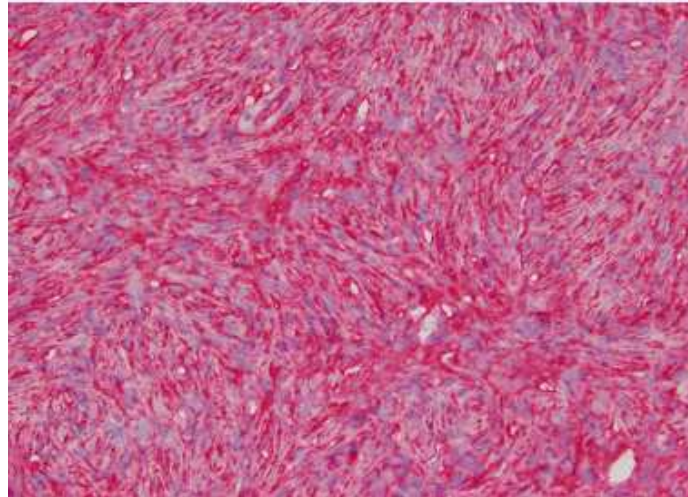
Rare soft tissue tumor, accounts for up to 1% of all soft tissue sarcomas.

### Clinics

Typically diagnosed in young to middle-aged adults and affects either sex and all races, however numerous pediatric and congenital cases have been reported. The duration of the lesions prior to diagnosis is commonly more than 5 years, and decades in some cases.



Typical dermatofibrosarcoma protuberans (H&E, 40x)



From top to bottom: a), b) Strong CD34 immunoreactivity (CD34, 40x).

### Pathology

Monotonous storiform pattern of uniform, cytologically bland spindle cells, with a characteristic honeycomb pattern of infiltration into the subcutaneous fat. Immunohistochemical staining demonstrates strong positivity for vimentin and CD34 and negativity for factor XIIIa staining. Apolipoprotein has also been described as a marker for DFSP.

### Treatment

Preferred treatment for DFSP is wide surgical excision with pathologically negative margins. Recently Imatinib mesylate therapy has been documented to induce extensive regression of primary and metastatic lesions.

### Prognosis

Despite the local invasiveness, DFSP rarely metastasizes. The risk for development of metastatic disease is only 5%. The extent of surgical excision determines the prognosis of the patient. To reduce the local recurrence rate, a wide surgical excision with adequate margins is used.

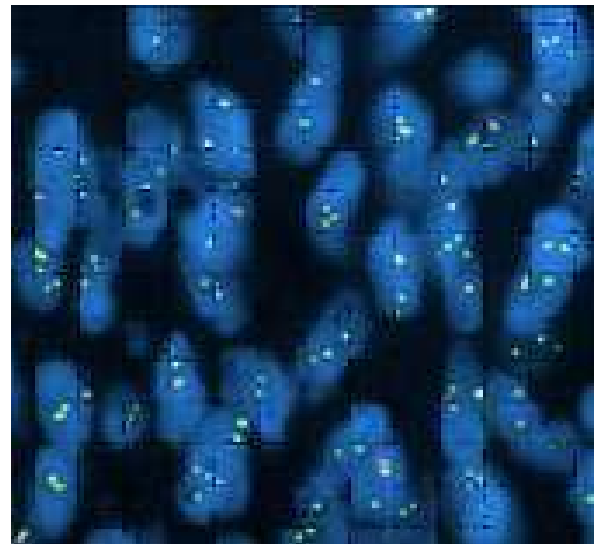
## Cytogenetics

### Cytogenetics Morphological

Cytogenetically, DFSP is characterized by the presence of the recurrent  $t(17;22)(q22;q13)$  translocation or, more commonly, supernumerary ring chromosomes containing material from chromosomal regions 17q22 and 22q13 accompanied by simple chromosome trisomies. The translocation results in the fusion of the alpha chain type 1 of collagen (COL1A1) gene with the platelet-derived growth factor Beta (PDGFbeta) gene.

### Cytogenetics Molecular

Fluorescence in situ hybridization based approaches can be used to demonstrate the  $t(17;22)$ , using gene specific probes to demonstrate PDGFbeta gene rearrangements as well as genetic gains and losses.



FISH of a DFSP case using a break-apart probe to the PDGFB locus shows tumor cells with one yellow signal indicating an intact PDGFB locus, and two or more green signals, representing additional copies of an unbalanced rearranged PDGFB locus (x100).

## Genes involved and proteins

### COL1A1

#### Location

17q21.31-q22

#### Note

Molecular location: from base pairs 45,616,456 to 45,633,999.

#### DNA / RNA

COL1A1 is transcribed from centromere to telomere at 17q21.31-q22. The mRNA sequence contains 5927 bp, comprising 52 exons and spans approximately 18 kb. Exons 5 to 49 encode the alpha helical domain.

#### Protein

The COL1A1 gene produces a component of type I collagen called the pro- $\alpha 1(I)$  chain. The Alpha1 (I)

chains of the type I collagen are synthesized as procollagen molecules containing amino and carboxy-terminal propeptides, which are removed by site-specific endopeptidase synthesizing the 1464 amino acid protein.

### **PDGFbeta**

#### **Location**

22q12.3-q13.1

#### **Note**

Molecular location: from base pairs 37,949,665 to 37,970,936.

#### **DNA / RNA**

The PDGFbeta mRNA sequence contains 3373 bp, comprising 7 exons and spans approximately 22 kb. Exon 7 and most part of the exon 1 are non-coding sequences.

#### **Protein**

The PDGFbeta chains are synthesized as 240 amino acids precursors molecules containing amino and carboxy-terminal propeptides, which are removed by site-specific endopeptidases. Two PDGFbeta precursor chains associate in dimers to form the mature PDGFBB after proteolysis.

## **Result of the chromosomal anomaly**

### **Fusion Protein**

#### **Note**

COL1A1 and PDGFbeta both encoded as pro-peptides are processed by proteolytic cleavage at N and C-terminus to give mature proteins. Sequences analyses of the chimerical COL1A1/PDGFbeta fusion transcripts has shown that the COL1A1/PDGFbeta putative proteins exhibit a pro-peptide structure, with a preserved N-terminus COL1A1 pro-peptide containing the signal peptide and the N and C-terminus PDGFbeta maturation cleavage sites. The result of this characteristic rearrangement of COL1A1 and PDGFbeta

is the transcriptional up-regulation of the PDGFB gene. The associated COL1A1-PDGFbeta fusion protein is posttranslationally processed to a functional PDGFbeta and results in PDGFbeta-mediated autocrine and/or paracrine activation of platelet-derived growth factor receptor-beta (PDGFBB).

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